Armed Forces College of Medicine

AFCM

Activation of B lymphocytes

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Humoral Immune response

By the end of this lecture the student will be able to*:*

1. Differentiate between the sequence of B cell activation in T cell dependent

   & T cell independent antigens

2. Compare between primary and secondary humoral immune response.

3.Discriminate between different isotypes of immunoglobulins regarding structure, distribution and function

4.Outline monoclonal Abs

B Cell receptor (BCR) complex

A Structure

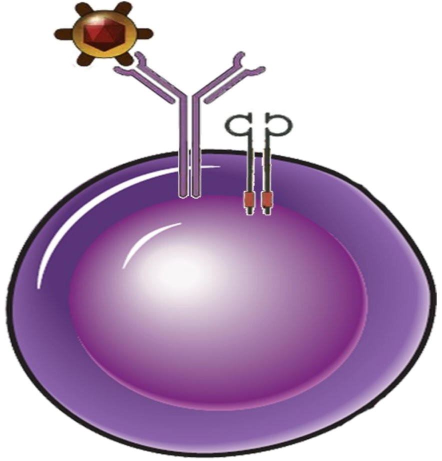
1) BCR: surface (membrane bound) IgM & IgD

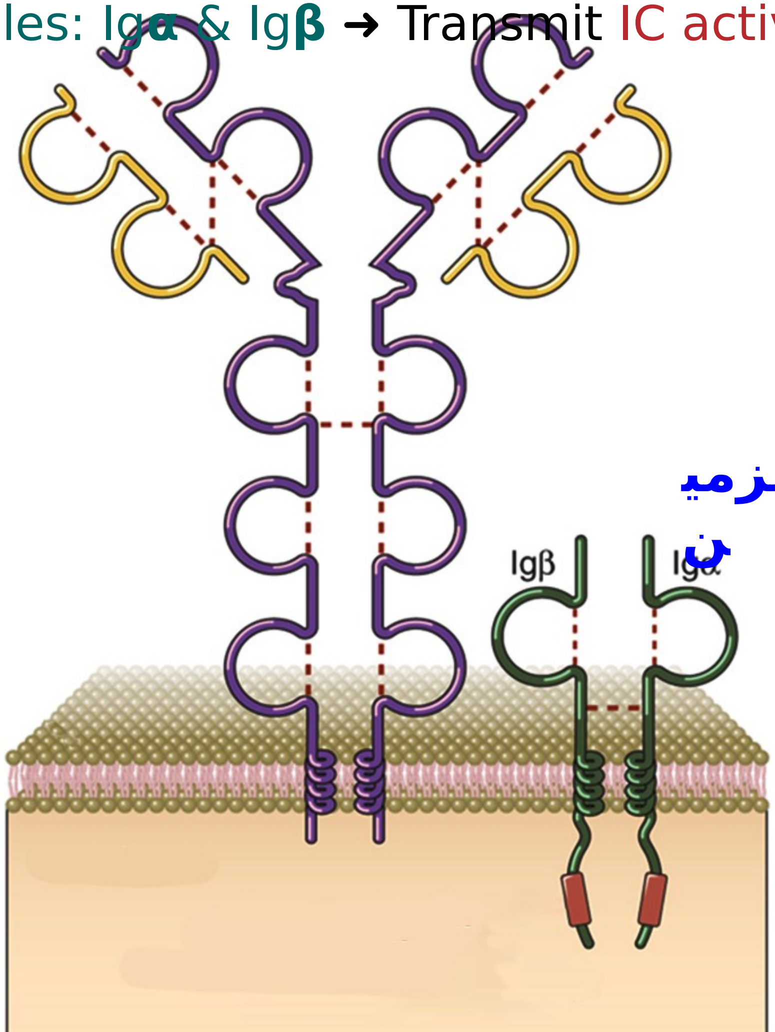
V (variable) region recognizes specific epitope (complementary to it)

رابطة بينية

2) 2 signaling molecules: Igα & Igβ ➜ Transmit IC activation signal

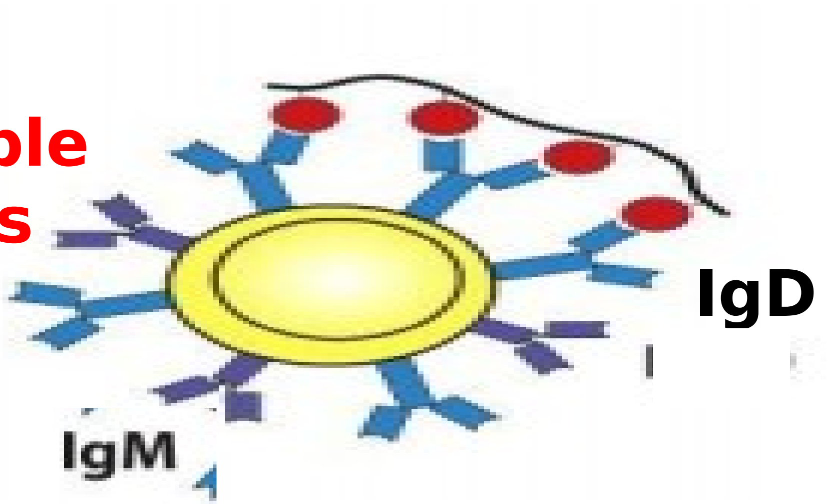
جزيئين الاشارة

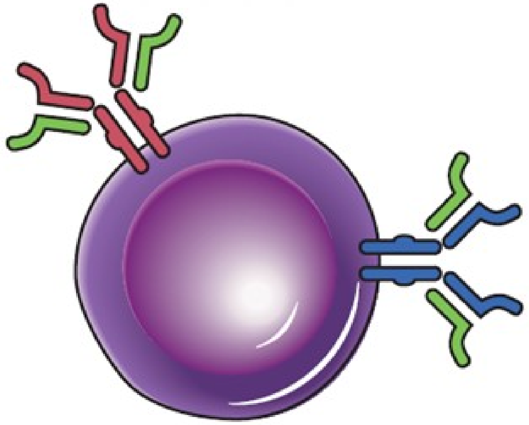




القزمين

Multiple BCRs

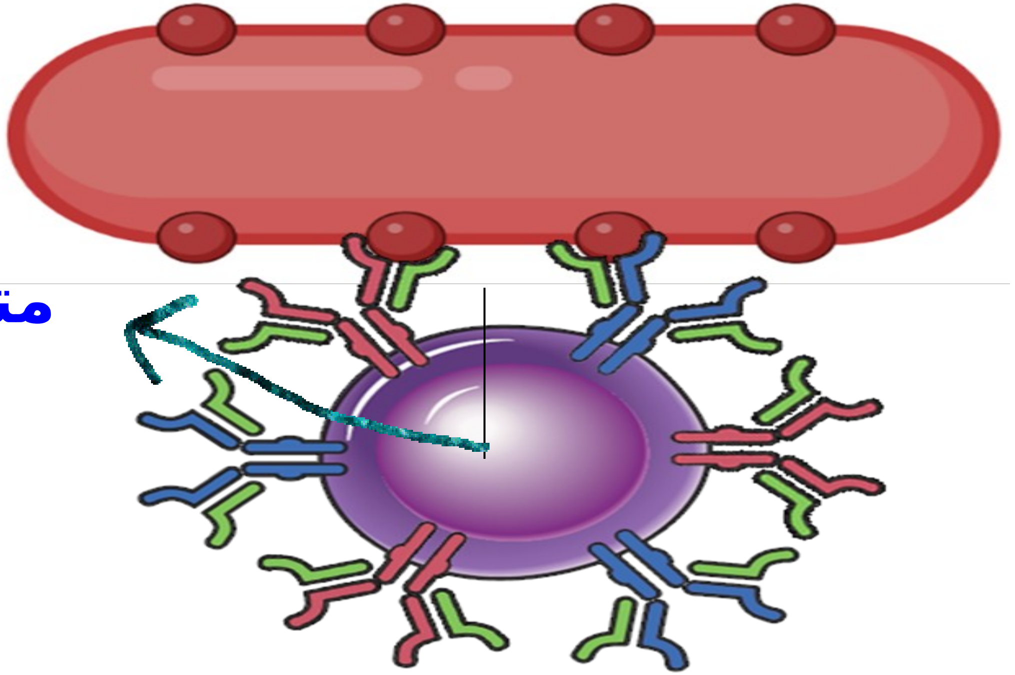




مقيدة

	B cell receptor
MHC restriction	**No** Recognize Ag without MHC protein
Ag characters	**1) Free (soluble) in its native form** **2) Proteins** **3) Polysaccharides & DNA**

هل هناك فرق بين
polysaccharides & proteins
في طريقة تحفيز **B cell**

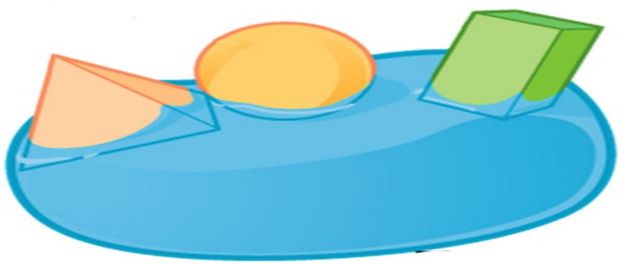


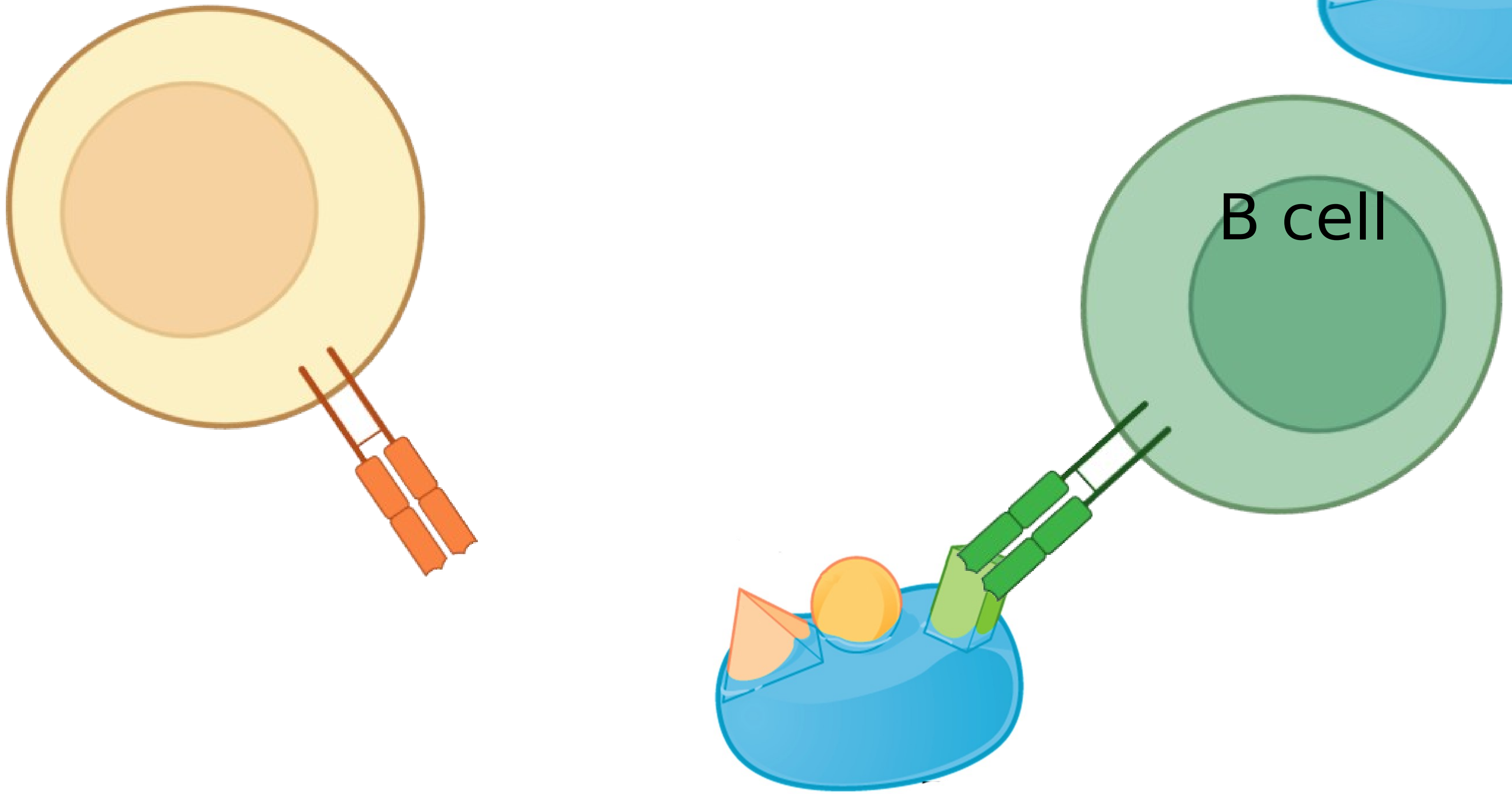
Functions of B cells

- ▶ Responsible for humoral immune response by producing Abs
- ▶ Professional Ag presenting cell (APCs)

➜ ⊕ Th cells

Epitope (antigenic determinant)





Definition

The smallest biochemical unit of Antigen that binds specifically with Ag receptor on B & T lymphocytes

↓

Stimulation of immune response

اصغر وحدة كيميائية

تحفيز الاستجابة

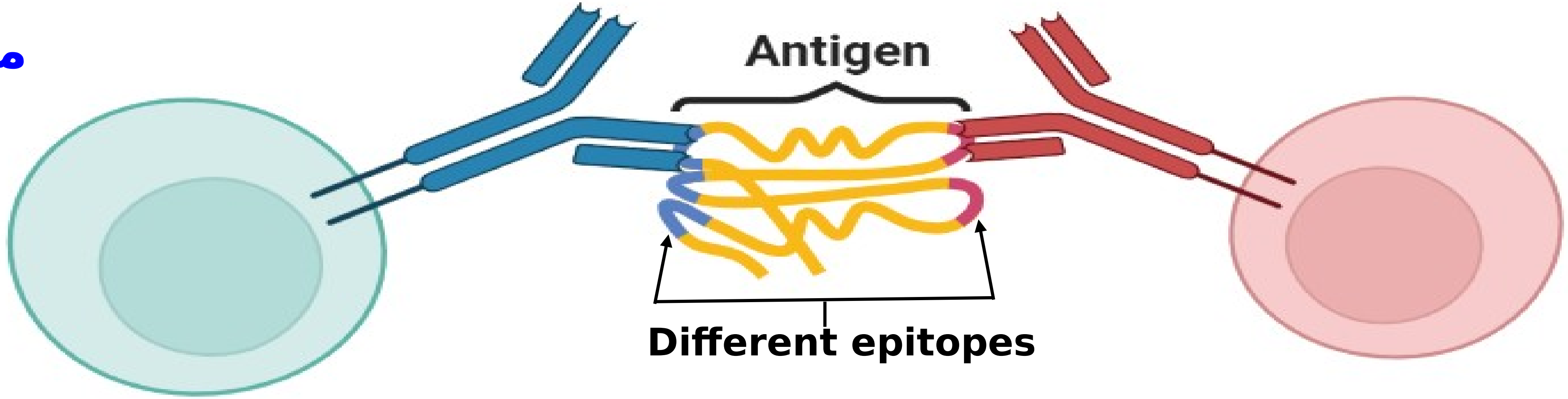
I - Protein Ags

1 Ag may have

يحفز نساءل مختلفة

- ▶ Several different epitopes Ag e.g protein → ⊕ different clones of B cells

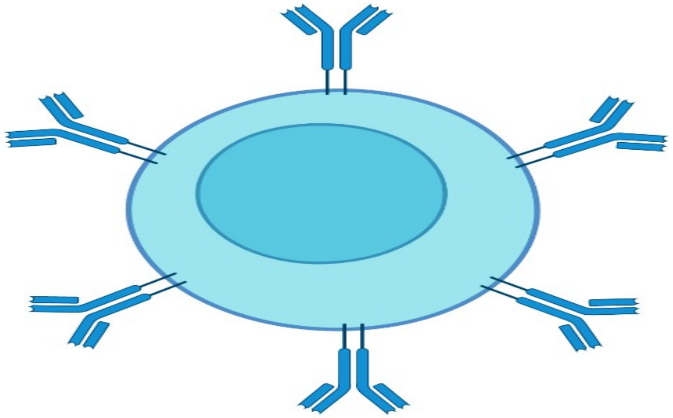
عديدة
مختلفة

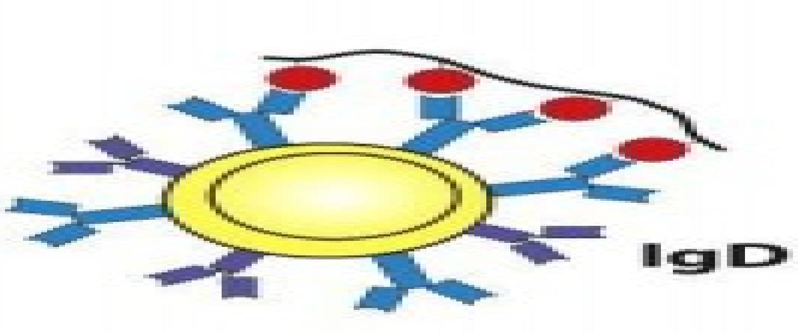


نسخة

نسخة
واحدة

NO Stimulation

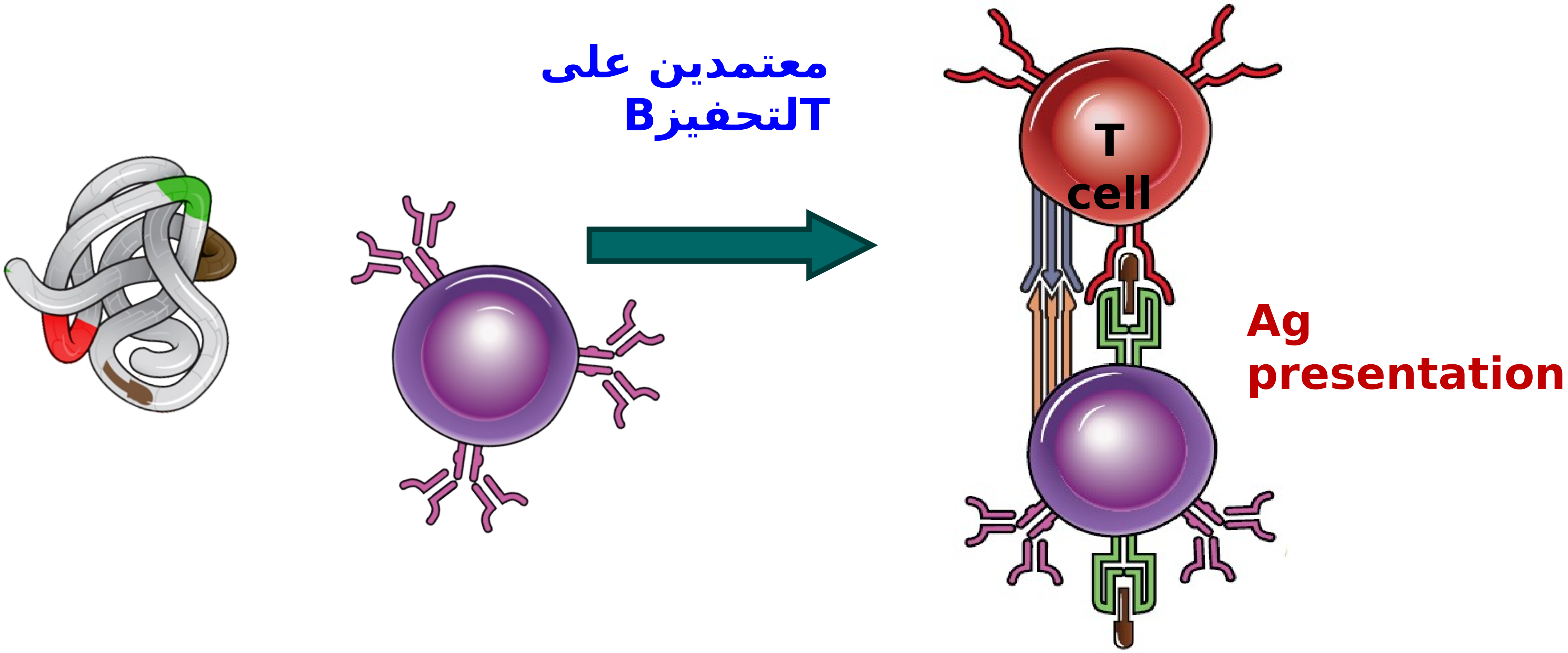




Activation of B cells

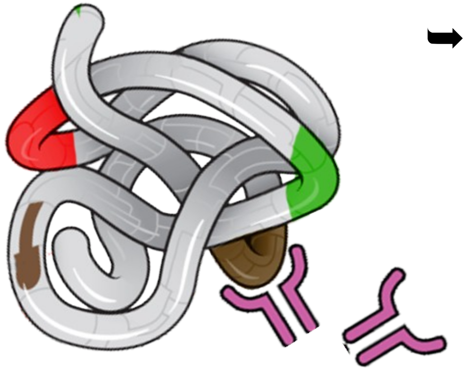
I - Protein Ags : T dependent Ags (thymus)

Need ⊕ of T helper cells to activate B cells → B cells will act as APCs to Th



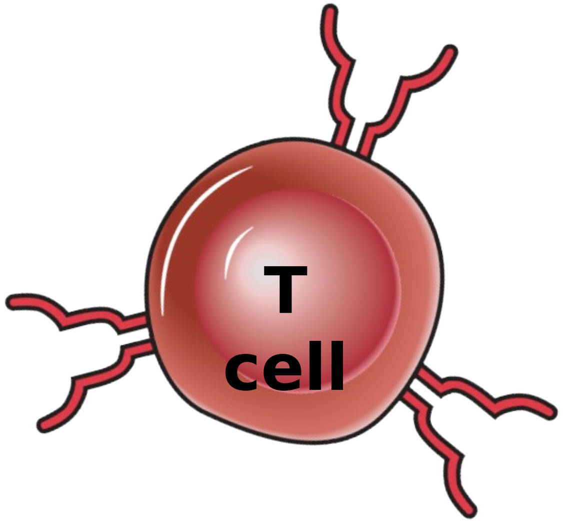
معتمدين على
التحفيزTB

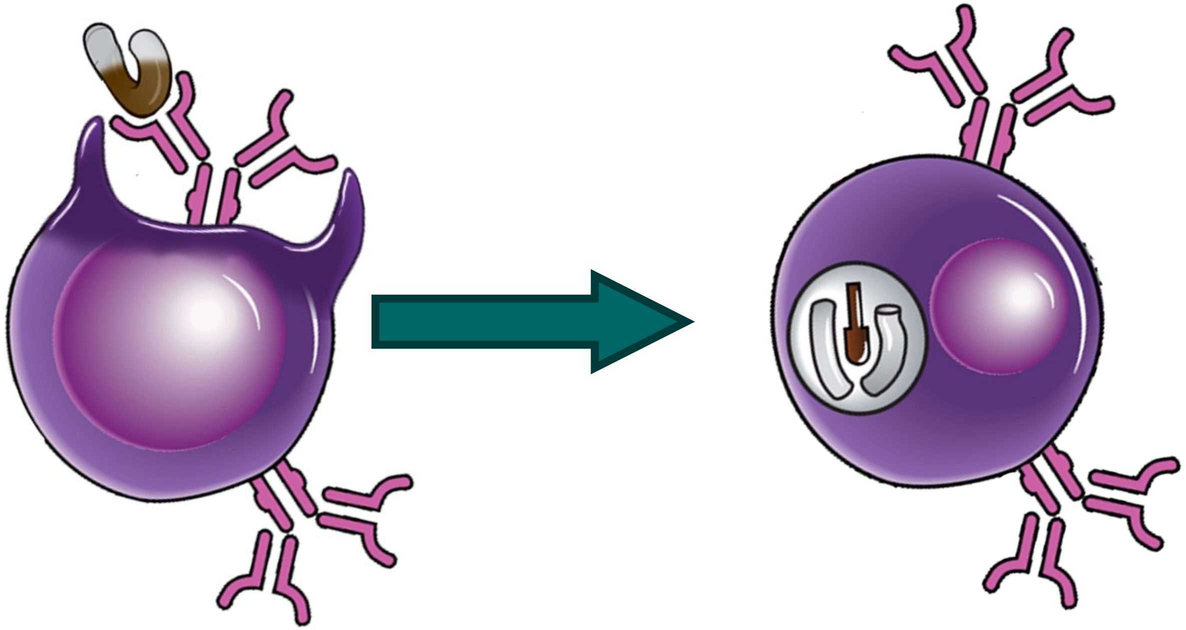
1 Ag binds to BCR (IgM or IgD)



➥ Internalized (receptor mediated endocytosis)

➥ Processed & epitopes are associated with MHC II proteins



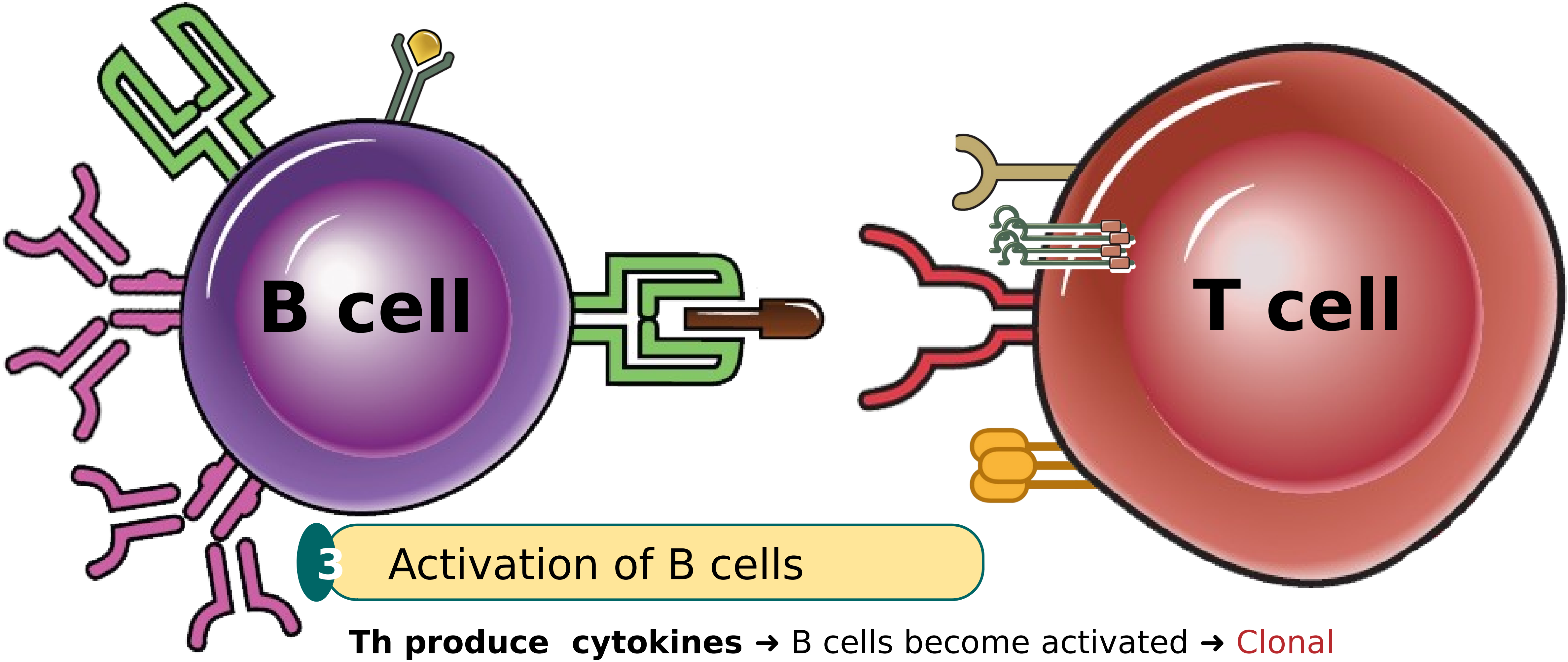


ادخال بواسطة
المستقبل

2 Interaction with activated Th cells

Peptide – MHC class II bind to TCR complex & CD4

Cytokines

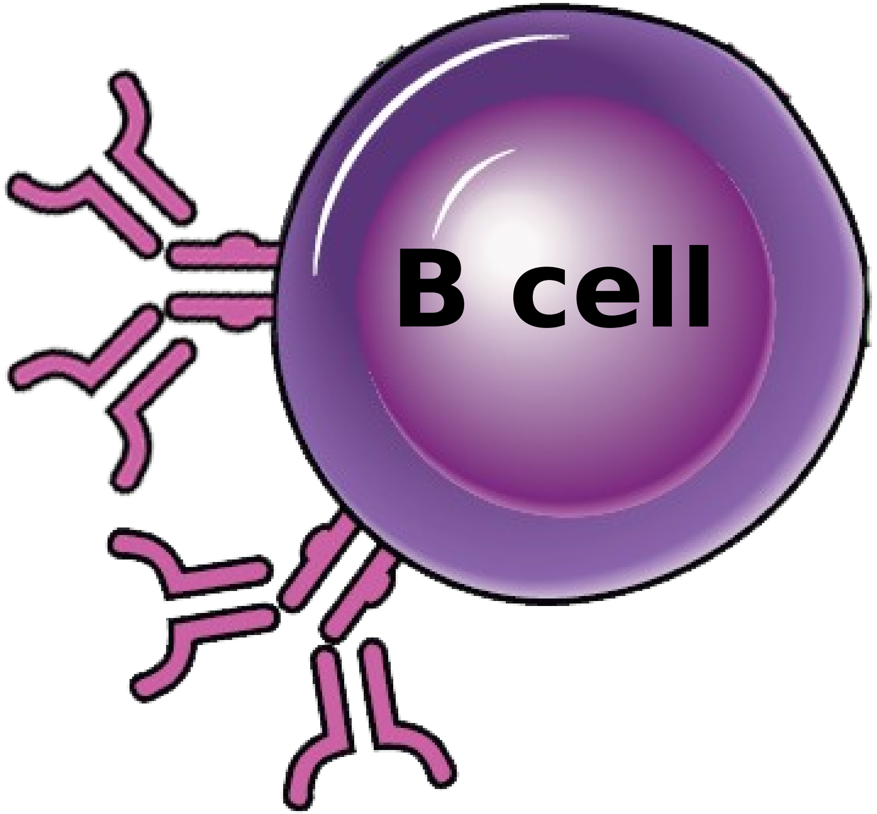


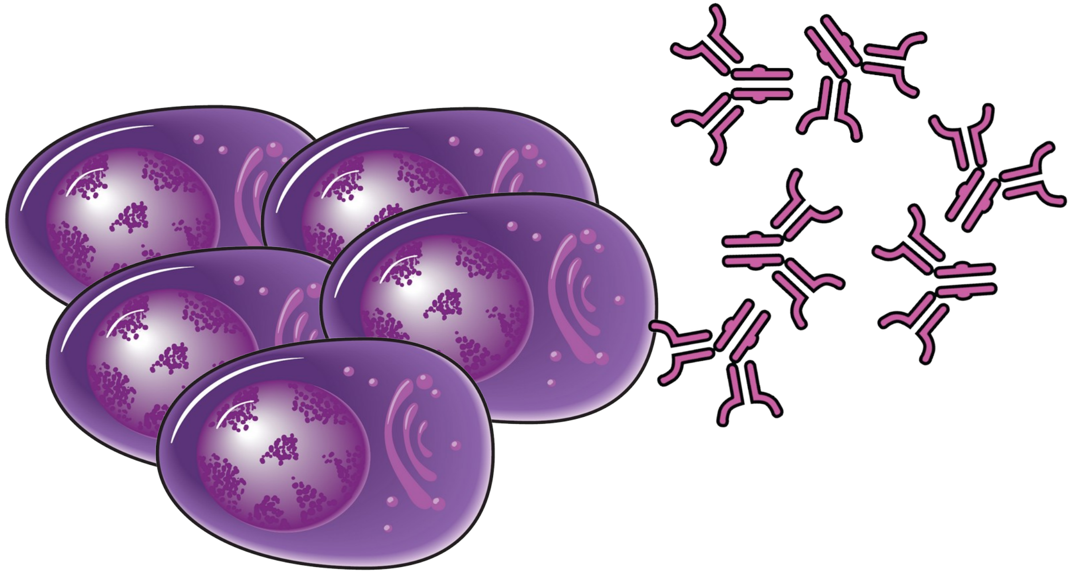
3 Activation of B cells

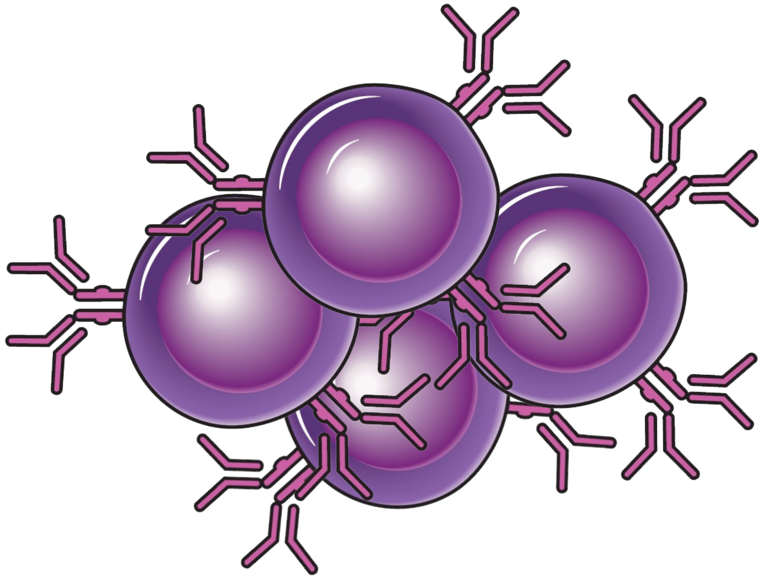
Th produce cytokines → B cells become activated → Clonal expansion

تمدد او تكاثر

4 Differentiation of activated B cells into



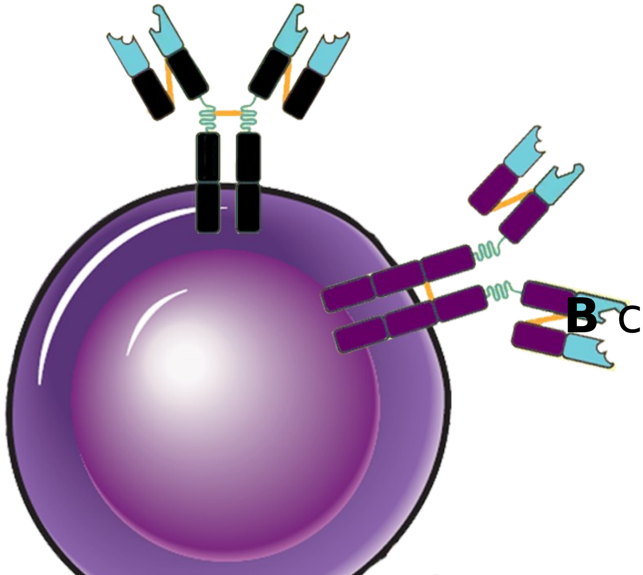




Remember

خصوصية
Specificity

Each clone of B cell will produce only 1 type of paratope (Variable)

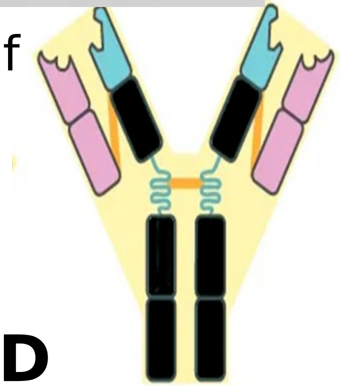


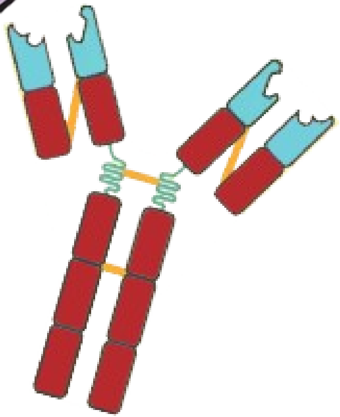
All 5 classes (isotypes)secreted from ***same clone*** of **B** cells :

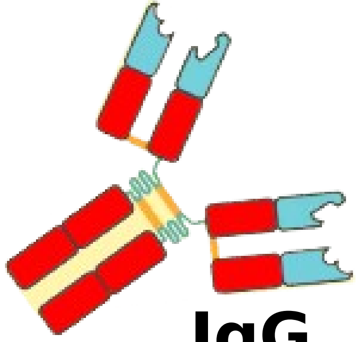
1) Have the same paratope (variable region)

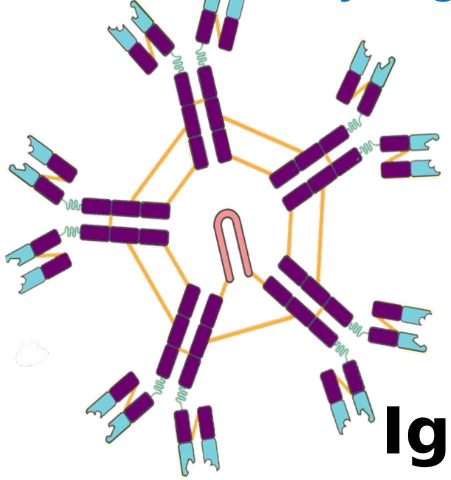
2) Are different in constant heavy region

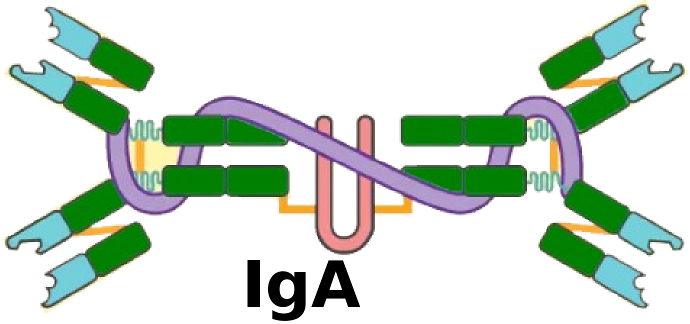
على حسب class


IgD


IgE


IgG


IgM


IgA

I - Protein Ags : T (thymus) dependent Ags

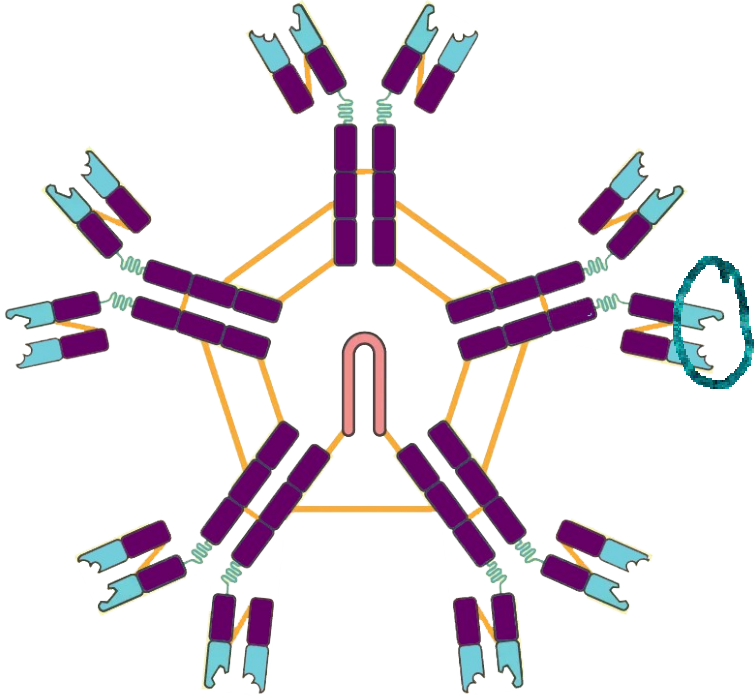
تحول

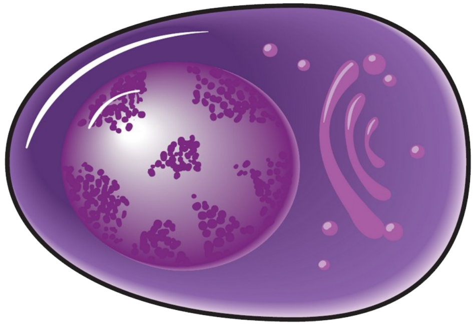
3 Differentiation of activated B cells into

A) Plasma cells

Produce Abs **specific for epitope**

1st Produce
IgM (secreted)





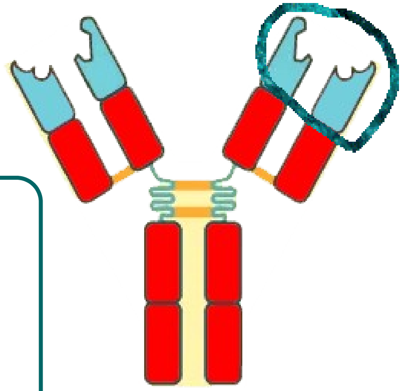
Change in the CH chain
↓
Production of another class of Ab while maintaining the same Ag specificity (same V)

تحافظ علي نفس خصوصية Ag

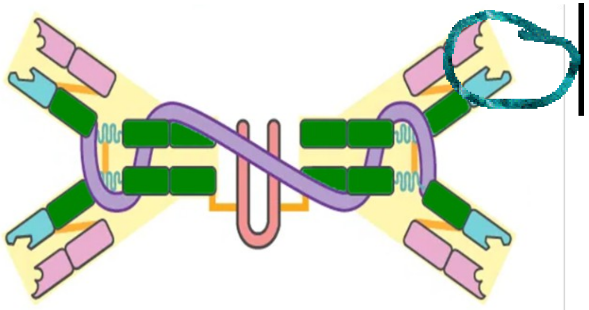
غير اللي تحت
و حافظ علي
اللي فوق

2nd : produce other classes by Isotype (class) switch

تحويل /تغيير



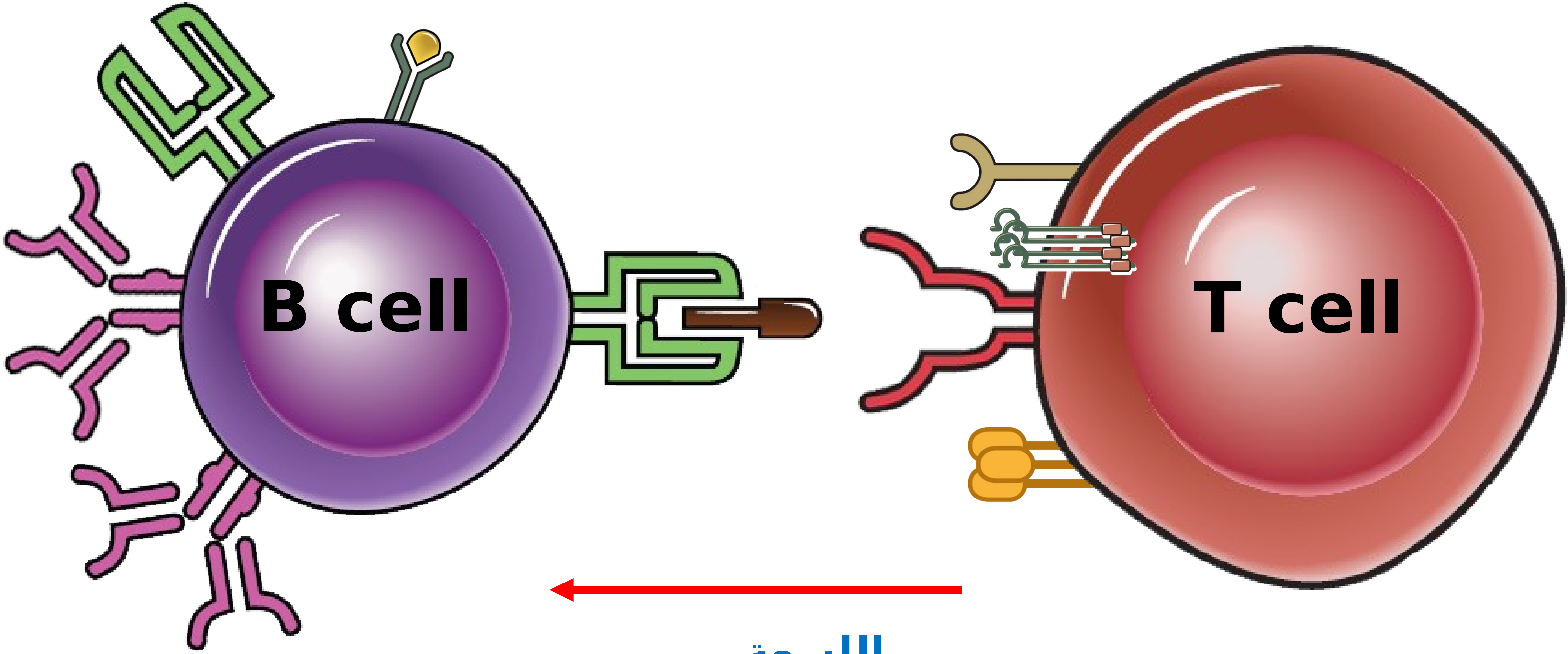
Same variable



Same variable

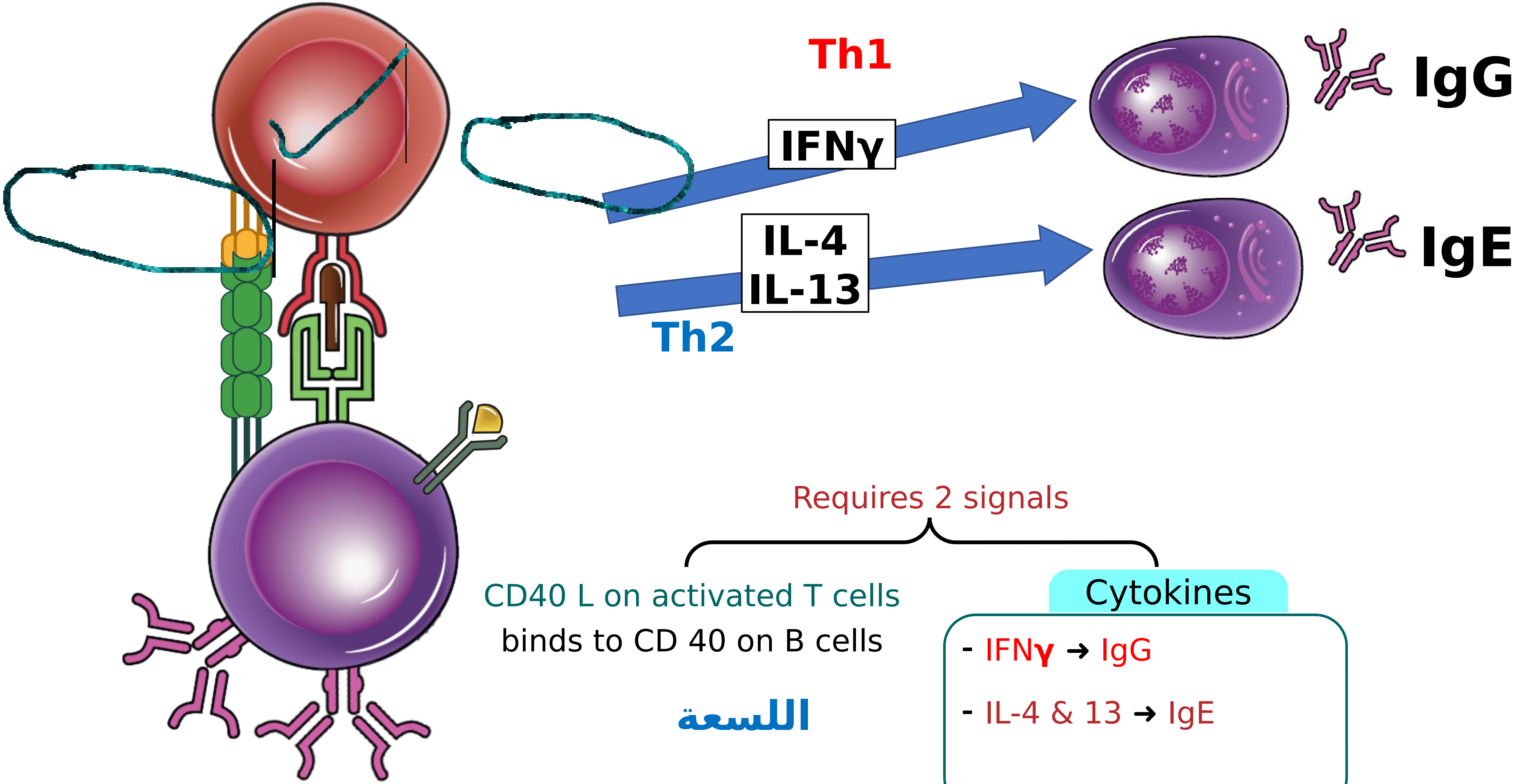
I - Protein Ags : T (thymus) dependent Ags

Requires 2 signals



اللسعة

I - Protein Ags : T (thymus) dependent Ags



Requires 2 signals

CD40 L on activated T cells
binds to CD 40 on B cells

اللسعة

Cytokines

- IFNγ → IgG
- IL-4 & 13 → IgE

B) Memory cells

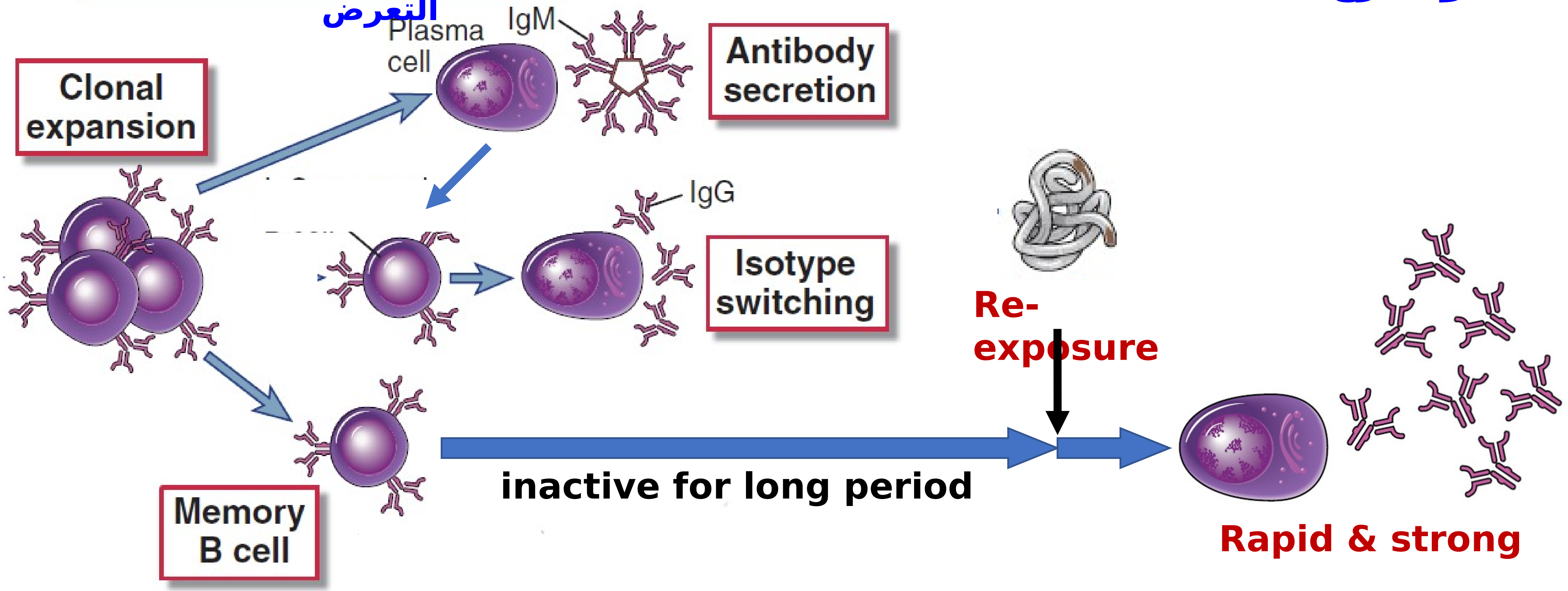
ساكنة

- **Remain inactive** for long periods

- **Activated rapidly** on re-exposure to same Ag → Rapid & Strong production of Abs

اقوى واسرع

اعادة التعرض



Clonal expansion

Antibody secretion

Isotype switching

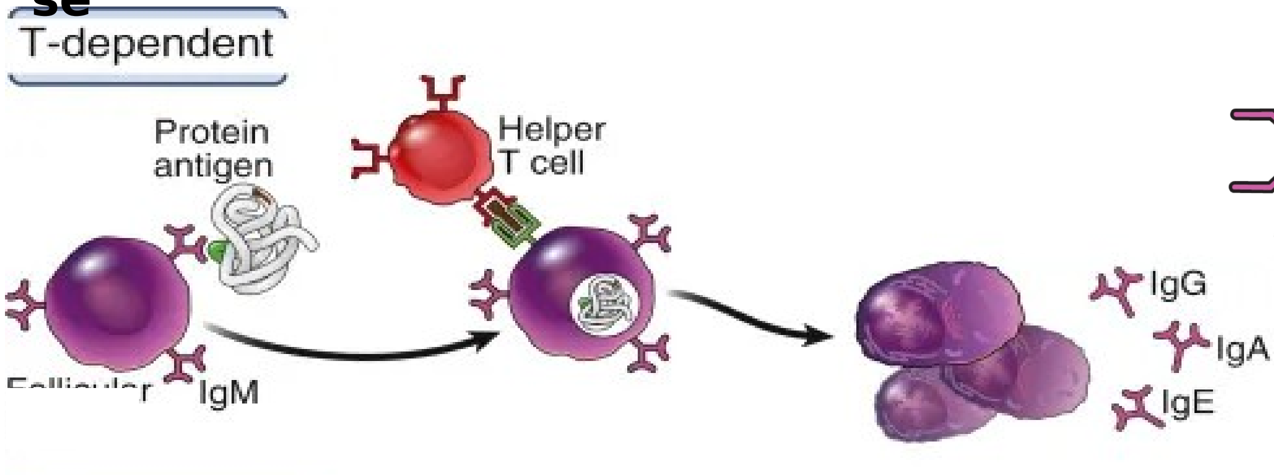
Memory B cell

inactive for long period

Re-exposure

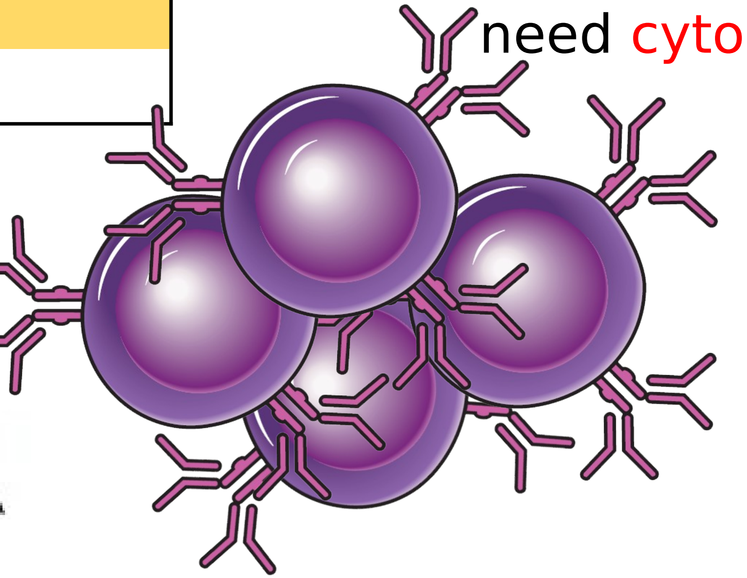
Rapid & strong

	T cell dependent Ags
Structure & Examples	Not formed of repeating epitopes e.g Proteins:
Characters of IR **Immune response**	1) Need ⊕ of Th cells (B cell acts as APC)
	2) Ab classes
	IgM & IgG, A , E (class switch)
	3) Memory response on 2nd exposure to same Ag
	Present



Formation of memory cells

need cytokines from Th



II) Polysaccharide Ags: T (Thymus) independent Ags

Epitope (antigenic determinant)

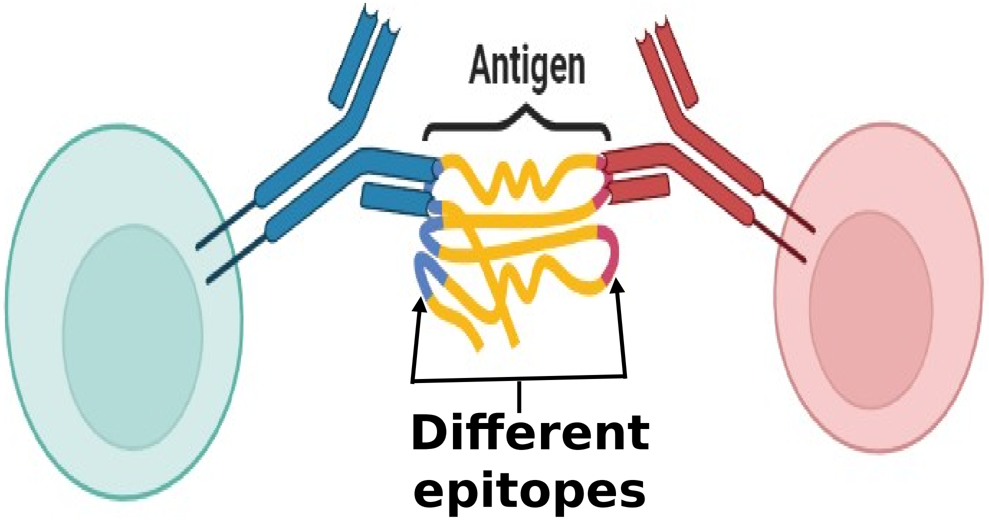
غير معتمدين على
T التحفيز B

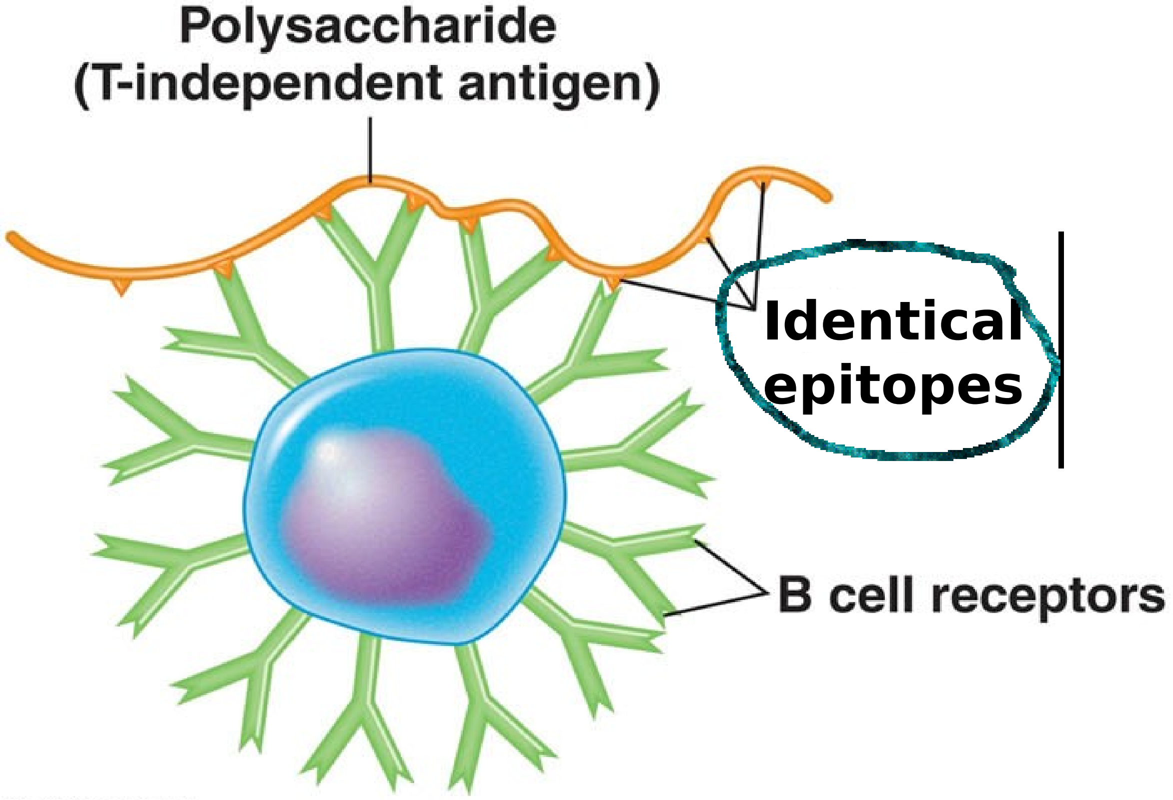
Activate B cells directly → **No need for Th**

1 Ag may have

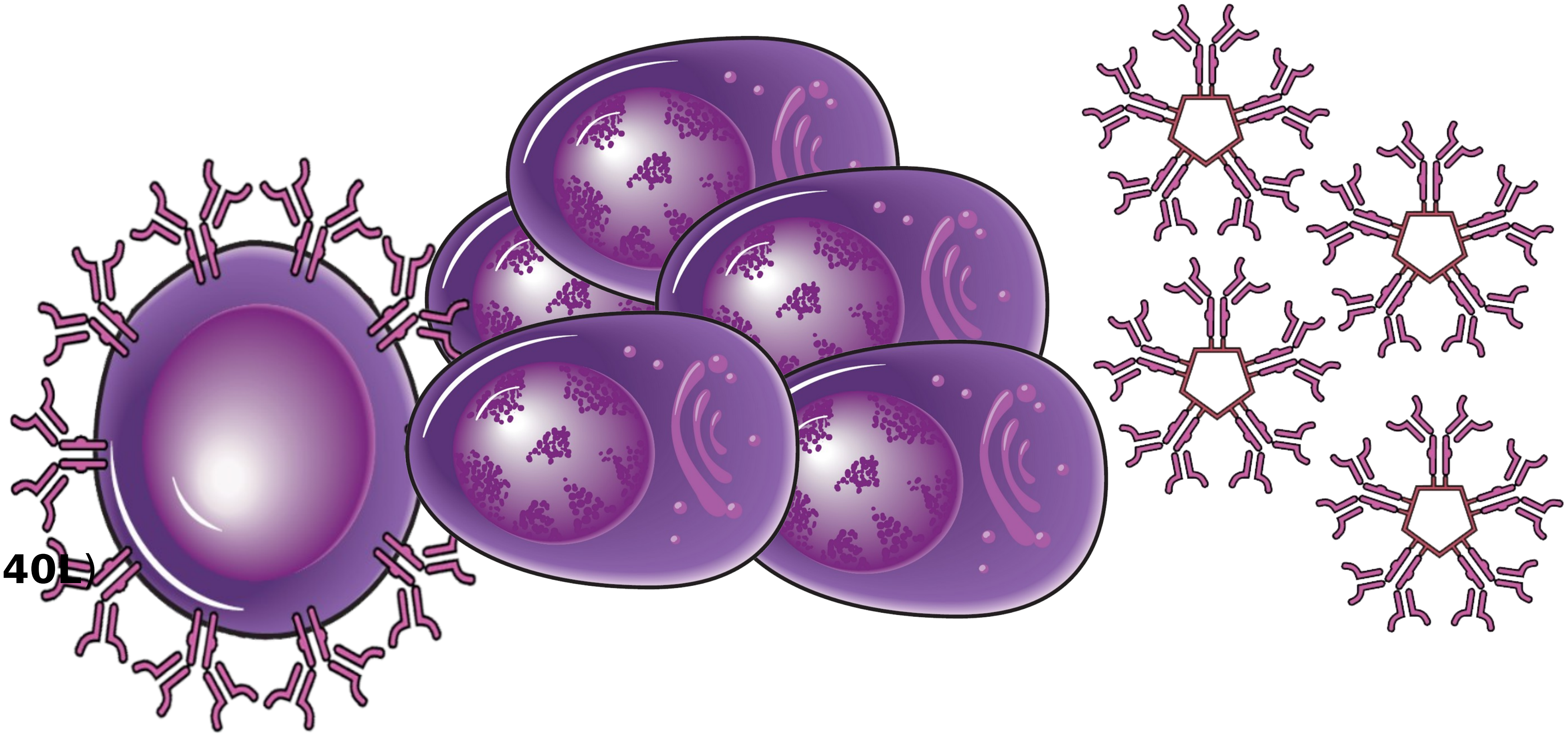
- Several different epitopes e.g protein Ag → ⊕ different clones of B cells
- Repeating (identical) epitopes e.g polysaccharide of bacteria → ⊕ the same (one) clone of B cell

متكررة متماثله





II) Polysaccharide Ags: T (Thymus) independent Ags



2) Ab classes : IgM only

(No class switch due to absence of cytokines & CD40L)

مفيش لسعة

1) Activate B cells directly by cross linking multiple BCRs

(No need for Th)

↓

Faster stimulation تحفيز

3) No Memory response on 2nd exposure to same Ag

Quiz 1

Which of the following characterizes bacterial capsules?

A. Induce production of IgG
B. On reexposure to them, the immune response will be faster
C. On reexposure to them, the immune response will be stronger
D. Are formed of multiple non repeating epitopes
E. Activate B cell directly without T cell help

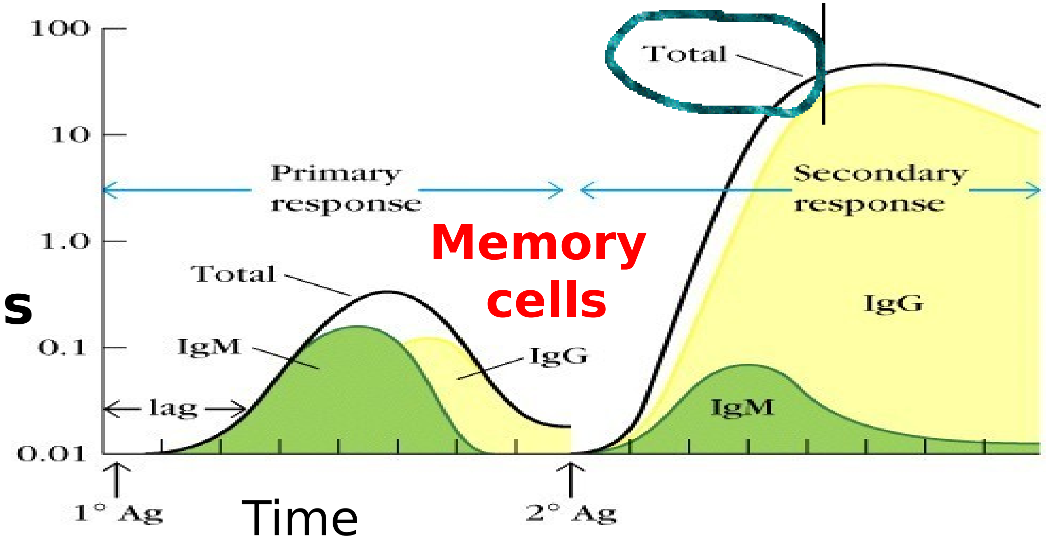
E

التعرض لاول مرة

1st exposure to Ag → استجابة مناعية اولية

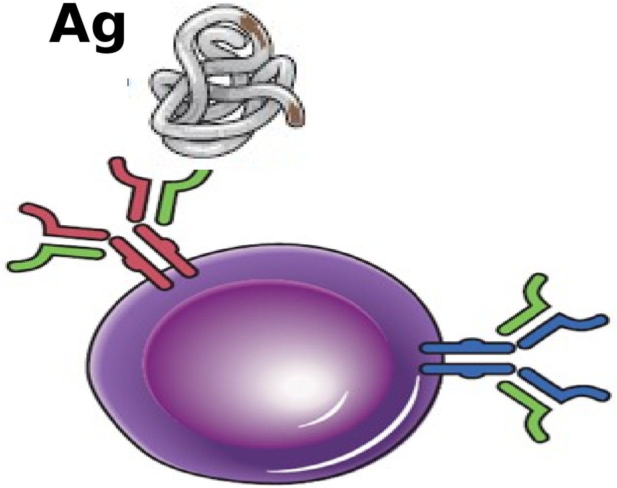
1ry Immune response

Level of Abs



Time

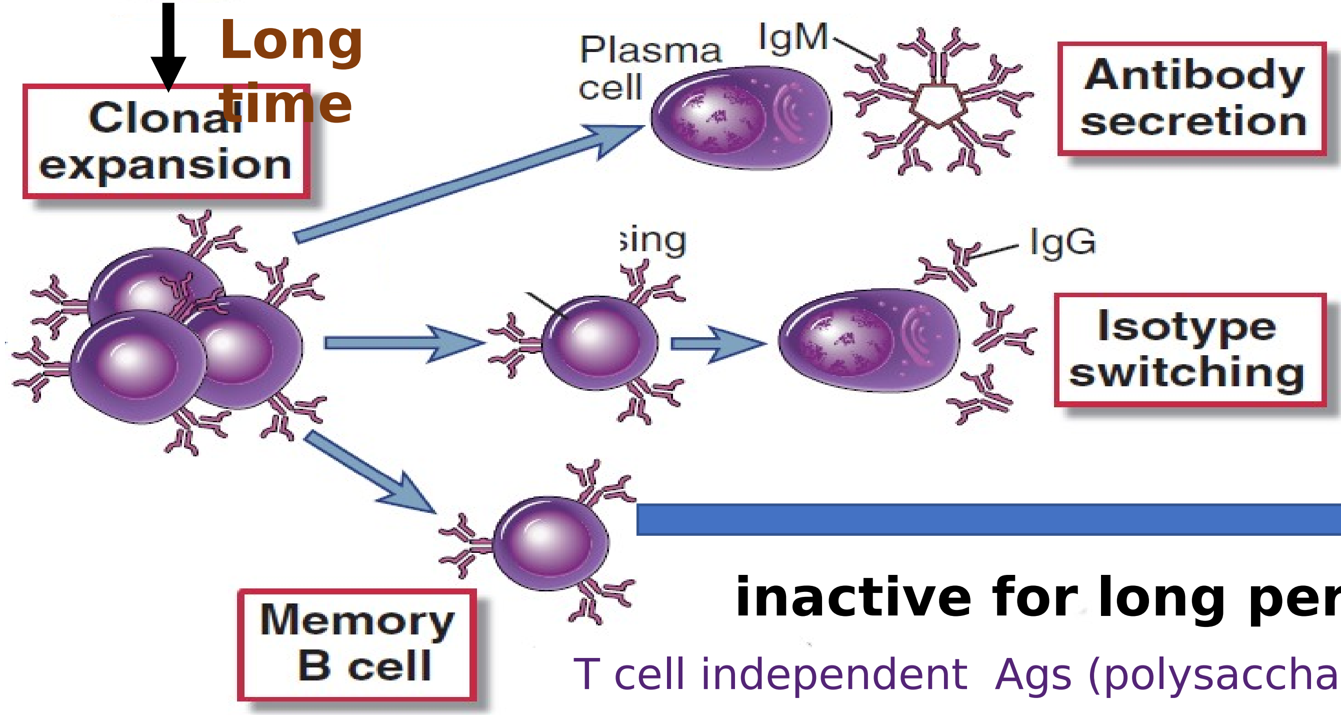
Memory cells



T cell dependent Ags

(Proteins)

Long time



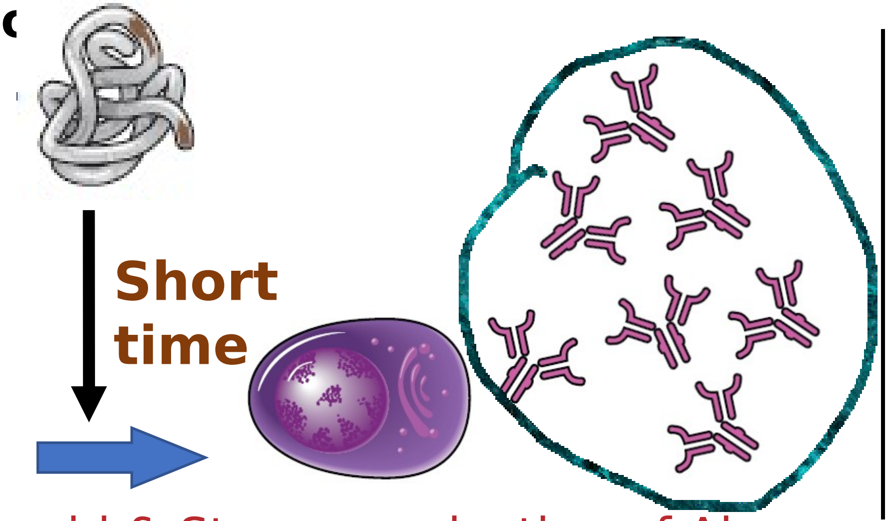
inactive for long period

T cell independent Ags (polysaccharides)

اعادة التعرض

Re-expo → الثانوية

2ry Immune response



Short time

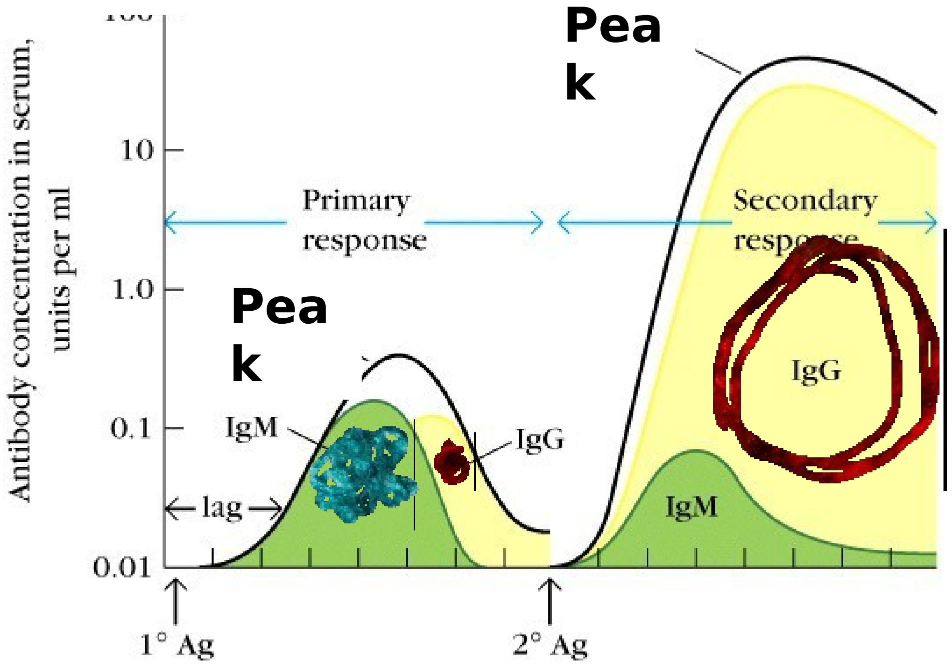
Rapid & Strong production of Abs

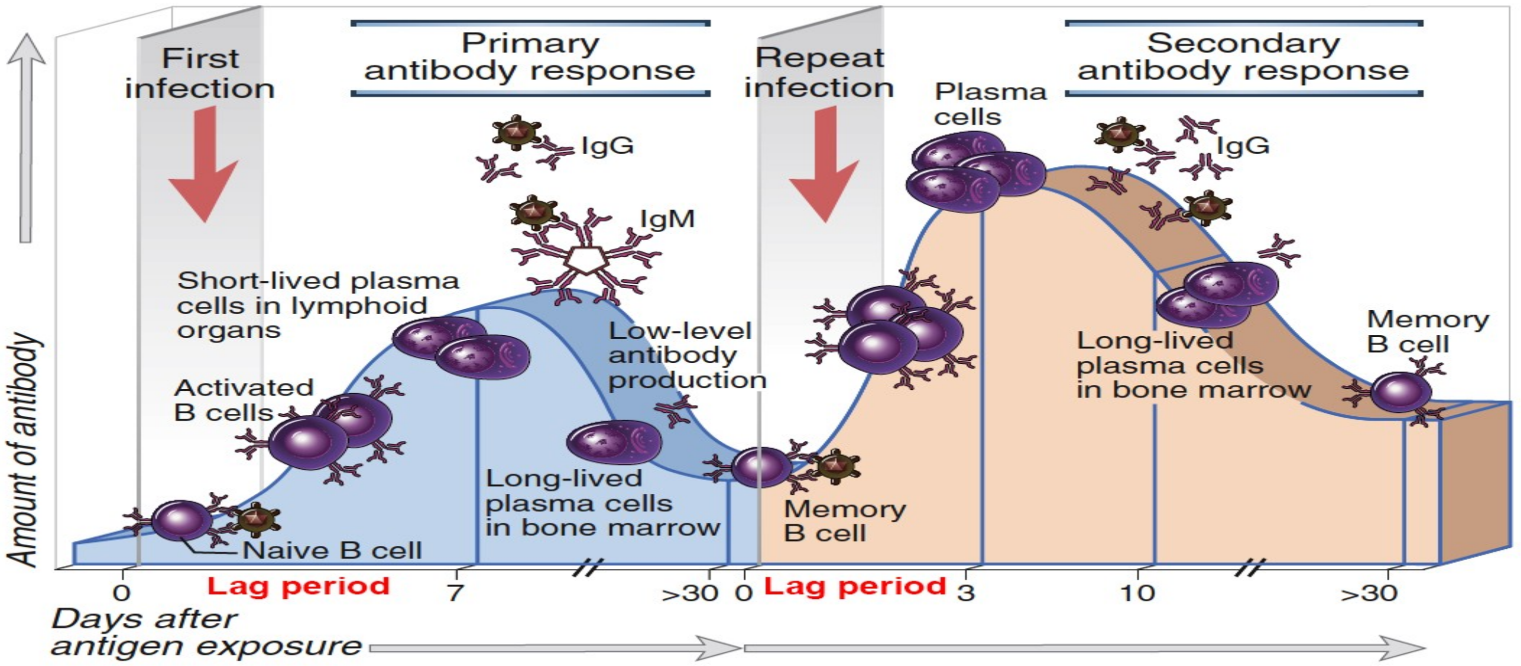
اقوى

	1ry Immune response	**2ry Immune response**
Ag	- 1st exposure to Ag - T cell dependent & independent Ags	- Reexposure to the same Ag - T cell dependent Ags only
Responding B cell	Naïve B cells	Memory B cells

المستجيبة

فترة التاخر	**1ry Immune response**	**2ry Immune response**
Lag period following Ag exposure	7- 10 days	1 – 3 days
Ab level (peak response)	تستمر في الزيادة لاسابيع Low: concentration continues to ↑ for several weeks ➜ very low levels مستويات منخفضة جدا	High (persists much longer) تستمر فتره اطول
Main isotype produced	IgM ينتج اولا ويختفي اولا (**1**st produced , but ↓ earlier than IgG)	IgG




First infection
Primary antibody response
Repeat infection
Secondary antibody response
Plasma cells
IgG
IgM
IgG
Short-lived plasma cells in lymphoid organs
Activated B cells
Low-level antibody production
Long-lived plasma cells in bone marrow
Naive B cell
Memory B cell
Long-lived plasma cells in bone marrow
Memory B cell
Amount of antibody
0
Lag period
7
>30
0
Lag period
3
10
>30
Days after antigen exposure

Practical applications of 2ry immune response

↓

Induction of memory cell

1- 2nd exposure to same microbe

↓

No disease

2-Vaccine (killed microbe)

↓

Exposure to **microbe (2nd exposure)** will activate **memory cells**